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PATENT
Customer No. 22,428
Attorney Docket No. 080618-0237

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: John P. Cooke et al.

Title: ENHANCEMENT OF VASCULAR FUNCTION BY MODULATION
OF ENDOGENOUS NITRIC OXIDE PRODUCTION OR ACTIVITY

Appln. No.: 10/618,835

Filing Date: 07/15/2003

Examiner: J. Russel

Art Unit: 1654

INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. § 1.97(b)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicants bring to the Examiner's attention the documents on the attached form PTO/SB/08. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

Non-English language documents

EP 0 511 118 A1 (C9): A Derwent Abstract of this document was filed in an IDS on May 19, 2004. According to the abstract, U.S. Pat. No. 5,352,695 (also filed May 19, 2004 as B2) is in the same family.

FR 2 507 892 (C14): Attached is UK Patent Application GB 2,100,982, in English, identified in Derwent abstract as the British counterpart application (C14a).

The documents submitted were cited in pleadings in the litigation known to the Office, and documents not submitted here are believed to be of record. The pleadings submitted with this paper are as follows:

1. October 13, 2003 Letter Brief from Dina Grinsphun to Judge Ware appending two opinions which affect Daily Wellness' motion for summary judgment;
2. Order Denying Defendant's Request that the Court Identify Terms At Issue; Setting Case Management Conference; Denying Without Prejudice Defendant's Motion for Summary Judgment;
3. Herbalife's Preliminary Invalidity Contentions served in *Unither v. Herbalife*;
4. Herbalife's Preliminary Invalidity Contentions served in *Herbalife v. Unither*;
5. Defendant Daily Wellness' Preliminary Invalidity Contentions Pursuant to Patent Local Rule 3-3;
6. Defendant Daily Wellness' Supplemental Preliminary Invalidity Contentions;

7. Defendant ANB's Preliminary Invalidity Contentions Pursuant to Patent Local Rule 3-3; and

8. Defendant ANB's Supplemental Preliminary Invalidity Contentions.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and Applicants determine that the cited documents are not "prior art" under United States law, then Applicants reserve the right to present to the Office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

The Commissioner is hereby authorized to charge any fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date 05-21-2004

By Sean A. Passino (45,943)
For

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

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MODIFIED PTO/SB/08 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
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Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

Date Submitted: May 21, 2004

(use as many sheets as necessary)

Sheet 1 of 15

Complete if Known

Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel

Attorney Docket Number 080618-0237

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
C1	2002/0091160	A1		COOKE, et al.	02-01-2002	
C2	5,026,721			DUDRICK, et al.	06-25-1991	
C3	5,028,627			KILBOURN, et al.	07-02-1991	
C4	6,117,872			MAXWELL, et al.	09-12-2000	
C5	6,337,321			COOKE, et al.	01-08-2002	
C6	6,552,074			KIMOTO, et al.	04-22-2003	
C7	6,646,006			COOKE, et al.	11-11-2003	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
C8	EP	0 259 167 A2			Millman	03-09-1988		
C9	EP	0 511 118 A1			N'Guyen	10-28-1992		
C10	EP	511 587 A1			Moriyama et al.	11-04-1992		
C11	EP	0 546 796 A1			Sonaka et al.	06-16-1993		
C12	WO	98/18491			Burgstiner	05-07-1998		
C13	ZA	9410015 A			Davis et al.	11-08-1995		
C14	FR	2 507 892			Brugioni et al.	12-24-1982		
C14a	GB	2 100 982			Brugioni et al.	06-22-1982		
C15	WO	85/00517			Niebes et al.	02-14-1985		

NON PATENT LITERATURE DOCUMENTS

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	C16	Adams et al., "Oral L-arginine improves endothelium-dependent dilatation and reduces monocyte adhesion to endothelial cells in young men with coronary artery disease" <i>Atherosclerosis</i> , 1997, 129(2):261-69.	
	C17	Adams et al., "Cigarette smoking is associated with increased human monocyte adhesion to endothelial cells: reversibility with oral L-arginine but not vitamin C," <i>J. Amer. Coll. Cardiol.</i> , 1997, 29(3):491-97.	

Examiner Signature

Date Considered

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				Examiner Name	J. Russel
				Attorney Docket Number	080618-0237

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	C18	Aimasheva et al., "Donor of nitric oxide improves, while NO-synthase inhibitor impairs resistance and adaptation to strenuous physical exercise," <i>Bulletin of Exp. Biol. and Med.</i> , 1998, 4:336-339.	
	C19	Aisaka et al., " ^N ^G -monomethyl-L-arginine, an inhibitor of endothelium-derived nitric oxide synthesis, abbreviates acetylcholine-induced vasodilatation in the guinea-pig" in <u>Nitric Oxide from L-arginine: a Bioregulatory System</u> (S. Moncada and E.A. Higgs, eds.), 1990, Chapter 40, pp. 379-384.	
	C20	Aisaka et al., "Modulation of cardiovascular function by L-arginine-derived nitric oxide" <i>Frontiers and new horizons in amino acid research</i> (K. Takai, ed.), 1992, 437-442.	
	C21	Aisaka et al., "Regulation of vascular resistance by L-arginine-derived nitric oxide," <i>J. Pharmacobio-Dyn.</i> , 1992, 15:s-60.	
	C22	Alba-Roth et al., "Arginine stimulates growth hormone secretion by suppressing endogenous somatostatin secretion," <i>J. Clin. Endocrinol. Metab.</i> , 1988, 67(6):1186-89.	
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	C24	Aoyama et al., "Effects on liver and serum lipids of dietary supplements of methionine and excess lysine given to previously-starved rats," <i>British J. Nutr.</i> , 1983, 50(3):627-36.	
	C25	Barbul et al., "Arginine" in <u>Nutrition in Critical Care</u> (Gary Zaloga ed.), 1994, Chapter 6, pp. 107-21.	
	C26	Barbul A., "Physiology and pharmacology of arginine" in <u>Nitric Oxide from L-Arginine:A Bioregulation System</u> (Moncada, S. and Riggs, E.A., eds.), 1990, Chapter 33, pp. 3 17-29.	
	C27	Barbul A., "Arginine and immune function," 1999, <i>Nutr.</i> 6(1):53-62.	
	C28	Barbul et al., "Arginine: a thymotropic and wound-healing promoting agent," 1977, <i>Surg. Forum.</i> 28:101-103.	
	C29	Barclay et al., "The role of blood flow in limiting maximal metabolic rate in muscle," 1975, <i>Med Sci Sports.</i> 7(2):I 16-119.	
	C30	Baumier et al., "Arginine: new and exciting developments for an 'old' amino acid," 1996, <i>Biomed. Environ. Sci.</i> 9(2-3):296-315.	
	C31	Bellamy et al., "Oral L-arginine improves exercise tolerance and flow-related endothelial dysfunction in microvascular angina," 1996, Abstract No. 2478, Suppl. <i>Circulation</i> 94(8):I-425.	

Examiner Signature	Date Considered
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
Date Submitted: May 21, 2004				Filing Date	07/15/2003
(use as many sheets as necessary)				First Named Inventor	John P. Cooke
Sheet	3	of	15	Group Art Unit	1654
				Examiner Name	J. Russel
				Attorney Docket Number	080618-0237

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	C32	Bissell, "Porphyria," Textbook of Medicine (ed. Wyngaarden and Smith), W.B. Saunders Co., Harcourt Brace Jovanovich Inc. Philadelphia, 1988, pp. 1182-89.	
	C33	Blomqvist, "Cardiovascular adaptations to physical training," 1983, Annu. Rev. Physiol. 45:169-89.	
	C34	Blum et al., "Oral L-arginine in patients with coronary artery disease on medical management," 2000, Circulation 101:2160-64.	
	C35	Bode-Boger et al., "Exercise increases systemic nitric oxide production in men," 1994, Cardiovasc. Risk. 1(2):173-78.	
	C36	Bode-Boger et al., "L-arginine infusion decreases peripheral arterial resistance and inhibits platelet aggregation in healthy subjects," 1994, Clin. Sci. (Lond) 87(3):303-10.	
	C37	Boger et al., "L-arginine increases nutritive muscular blood flow determined by positron emission tomography (PET) in patients with peripheral arterial occlusive disease," 1996, Abstract No. 3176, Suppl. Circulation 94(8):1-543.	
	C38	Böger et al., "Dietary L-arginine reduces the progression of atherosclerosis in cholesterol-fed rabbits: comparison with lovastatin," 1997, Circulation 96(4):1282-90.	
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	C44	Castillo et al., "Endothelium-dependent vasodilatation in rat aorta is mainly mediated by nitric oxide" Proc. West. Pharmacol Soc. 1997, 40:39-40.	

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	C45	Castillo et al., "Dietary arginine uptake by the splanchnic region in adult humans" Am J Physiol. 1993, 65(4 Pt 1):E532-39.	
	C46	Castillo et al., "Splanchnic metabolism of dietary arginine in relation to nitric oxide synthesis in normal adult man" Proc. Natl. Acad. Sci. USA 1993, 90(1):193-97.	
	C47	Castillo et al., "Plasma arginine and citrulline kinetics in adults given adequate and arginine-free diets" Proc. Natl. Acad. Sci. USA 1993, 90:7749-53.	
	C48	Castillo et al., "Plasma arginine kinetics in adult man: response to an arginine-free diet" Metabolism 1994, 43(1):114-22.	
	C49	Ceremuzkynski et al., "L-arginine improves exercise capacity in patients with stable angina" Supplement to J. of Am. College of Cardiology, 1997, 29(2): Supp. A. Abstract 962-94.	
	C50	Ceremuzynski et al., "Effect of supplemental oral L-arginine on exercise capacity in patients with stable angina pectoris" Am. J. Cardiol. 1997, 80(3):331-33.	
	C51	Chauhan et al., "Aging-associated endothelial dysfunction in humans is reversed by L-arginine" J. Amer. Coll Cardiol. 1996, 28(7):1796-1804.	
	C52	Chen et al., "L-arginine prevents hypertension in salt-sensitive (SS/Jr) Dahl/Rapp rats" Clinical Research 1991, 39:379A.	
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	C55	Cheng et al., "L-arginine in the management of cardiovascular diseases" Ann Pharmacother, 2001, 35(6):755-64.	
	C56	Chester et al., "Low basal and stimulated release of nitric oxide in atherosclerotic epicardial coronary arteries" Lancet 1990, 336(8720):897-900.	
	C57	Chester et al., "The role of nitric oxide in mediating endothelium dependent relaxations in the human epicardial coronary artery" Int J Cardiol. 1990, 29(3):305-09.	

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	C58	Church et al., "Hypertension and renal impairment as complications of acute porphyria" Nephrol Dial Transplant. 1992, 7(10):986-90.	
	C59	Cooke et al., "Endothelial dysfunction in hypercholesterolemia is corrected by L-arginine" Basic Res Cardiol., 1991, 86 Suppl 2:173-81.	
	C60	Cooke J.P., "A peculiar result and a fanciful hypothesis regarding L-arginine" Atheroscler. Thromb. Vasc. Biol. 2003, 23:1128-31.	
	C61	Creager et al., "L-arginine improves endothelium-dependent vasodilation in hypercholesterolemic humans" Supplement to Circulation 1990, 82:III-346, 1248-1253.	
	C62	Cynober et al., "Arginine metabolism in mammals" J. Nutr. Biochem. 1995, 6:402-13.	
	C63	Davies et al., "Combination therapy of cholesterol reduction and L-arginine supplementation controls accelerated vein graft atheroma" Ann. Vasc. Surg. 1999, 13(5):484-93.	
	C64	de Graaf JC et al., "Nitric oxide functions as an inhibitor of platelet adhesion under flow conditions". Circulation 1992, (6):2284-90.	
	C65	Deguchi et al., "L-Arginine identified as an endogenous activator for soluble guanylate cyclase from neuroblastoma cells".J. Biol. Chem. 1982, 257(17):10147-51.	
	C66	Dhanakoti et al., "Net renal arginine flux in rats is not affected by dietary arginine or dietary protein intake" Nutrient Metabolism 1992, 122(5):1127-34.	
	C67	Dubois-Rande, Jean-Luc et al., "L-arginine improves endothelium-dependent relaxation of conductance and resistance coronary arteries in coronary artery disease" J. of Cardio Pharm. 1992, 20(Suppl. 12):S211-S213.	
	C68	Edmonds et al., "Urea cycle metabolism: effects of supplemental ornithine or citrulline on performance, tissue amino acid concentrations and enzymatic activity in young pigs fed arginine-deficient diets" Anim. Sci. 1987, 65(3):706-16.	
	C69	Eklund et al., "Effects of the Source of Dietary Protein on Serum Lower Density Lipoprotein (VLDL + LDL) and Serum Tocopherol Levels in Female Rats" J. Nutr. 1980, 110(12):2321-35.	
	C70	Elder et al., "The acute porphyrias" Lancet. 1997 349(9065):1613-17.	
	C71	Elder et al., "Treatment of acute porphyria" Hosp Med. 2001, 62(7):422-25.	

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	C72	Feng Q., et al., "Endothelium-derived relaxing factor (EDRF) and nitric oxide (NO). I. Physiology, pharmacology and pathophysiological implications" Clin. Physiol. 1990, (5):407-26.	
	C73	Freiman et al., "Atherosclerosis impairs endothelium-dependent vascular relaxation to acetylcholine and thrombin in primates," Circ Res. 1986, 58(6):783-89.	
	C74	Frick et al., "Cardiovascular dimensions and moderate physical training in young men" J Appl. Physiol. 1970, 29(4):452-55.	
	C75	Furchtgott et al., "Interactions of endothelial cells and smooth muscle cells of arteries" Chest. 1985, 88(4 Suppl):210S-213S.	
	C76	Martin et al., "Depression of contractile responses in rat aorta by spontaneously released endothelium-derived relaxing factor" Pharmacol. Exp. Ther. 1986, 237(2):529-38.	
	C77	Furchtgott et al., "Evidence for endothelium-dependent vasodilation of resistance vessels by acetylcholine" Blood Vessels. 1987, 24(3):145-49.	
	C78	Furchtgott et al., "Evidence supporting the proposal that endothelium-derived relaxing factor is nitric oxide" Thrombosis Research 1987, Supp. VII:5.	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
Date Submitted: May 21, 2004				Filing Date	07/15/2003
(use as many sheets as necessary)				First Named Inventor	John P. Cooke
Sheet	7	of	15	Group Art Unit	1654
				Examiner Name	J. Russel
				Attorney Docket Number	080618-0237

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Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	C86	Furchgott, RF, "The role of endothelium in the responses of vascular smooth muscle to drugs" Ann. Rev. Pharmacol. Toxicol. 1984, 24:175-97.	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
Date Submitted: May 21, 2004				Filing Date	07/15/2003
(use as many sheets as necessary)				First Named Inventor	John P. Cooke
Sheet	13	of	15	Group Art Unit	1654
				Examiner Name	J. Russel
				Attorney Docket Number	080618-0237

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	C168	Sanchez et al., "Plasma amino acids and the insulin/glucagon ratio as an explanation for the dietary protein modulation of atherosclerosis" Medical Hypotheses 1991, 35:324-29.	
	C169	Schaffer et al., "Nitric oxide regulates wound healing" J. Surg. Res. 1996, 63(1):237-40.	
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	C182	Togashi et al., "A central nervous system action of nitric oxide in blood pressure regulation" J. Pharmacol. Exp. Ther. 1992, 262(1):343-47.	
	C183	Umans et al., "Nitric oxide in the regulation of blood flow and arterial pressure" Annu. Rev. Physiol. 1995, 57:771-790.	
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	C190	Vanhoutte et al., "Modulation of vascular smooth muscle contraction by the endothelium" Annu. Rev. Physiol. 1986, 48:307-20.	
	C191	Venho et al., "Arginine intake, blood pressure, and the incidence of acute coronary events in men: the Kuopio Ischaemic Heart Disease Risk Factor Study" Am. J. Clin. Nutr. 2002, 76:359-64.	
	C192	Volin et al., "Heme arginate: effects on hemostasis" Blood 1988, 71(3):625-28.	
	C193	von der Leyen HE, et al., "Gene therapy inhibiting neointimal vascular lesion: in vivo transfer of endothelial cell nitric oxide synthase gene" Proc. Natl. Acad. Sci. USA 1995 92(4):1137-41.	
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	C195	Waller et al., "Conditions for synthesis of antioxidative arginine-xylose maillard reaction products" Synthesis of Antioxidative Products 1983, pp. 125-40.	

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	C196	Wang et al., "Dietary arginine prevents atherogenesis in the coronary artery of the hypercholesterolemic rabbit" J Am College Cardiol. 1994, 23(2):452-58.		
	C197	Wascher, "Oral L-arginine supplementation in chronic heart failure" Circulation 1997, 95(6):1674-75.		
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	C201	Windmueller et al., "Source and fate of circulating citrulline" Am. J. Physiol. 1981 241(6):E473-80.		
	C202	Wu et al., "Arginine metabolism: nitric oxide and beyond" Biochem. J. 1998 336:1-17.		
	C203	Wu et al., "Arginine nutrition and cardiovascular function" Am. Society Nutr. Sci. 2000, 130:2626-29.		
	C204	Zeiher et al., "Modulation of coronary vasomotor tone in humans. Progressive endothelial dysfunction with different early stages of coronary atherosclerosis" Circulation 1991 83(2):391-401.		
	C205	Zeiher et al., "Endothelial Dysfunction of the Coronary Microvasculature Is Associated With Impaired Coronary Blood Flow Regulation in Patients With Early Atherosclerosis" Circulation 1991, 84(5):1984-92.		
	C206	Dialog Search Result for Normosang Synonyms. Chemsearch Database.		
	C207	European Porphyria Initiative, http://www.porphyria-europe.com , selected pages.		
	C208	Stedman's Medical Dictionary, The Williams and Wilkins Co. (23 rd Edition 1976), p. 1124.		

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